REMARKS/ARGUMENTS

Upon entry of this amendment, claims 4, 9-10, 12 and 17-18 will be pending in this application and presented for examination. Claims 4 and 9 have been amended. Claims 6, 7, 13 and 15 have been canceled. Claims 17-18 are allowable. No new matter has been entered with the foregoing amendments. Reconsideration is respectfully requested.

I. FORMALITIES

In this amendment, the features of claims 6 and 7 have been incorporated into claim 4, and the *ionic compound* therein has been restricted to a *cationic compound* having an ammonium, pyridinium, phosphonium, or sulfonium group in the molecule. In accordance with this revision, claims 6, 7, 13 and 15 have been canceled without prejudice. Thus, the features of the "ionic compound is incorporated at least in an equimolar amount based on the ionic prostaglandin I_2 derivative" and "anionic prostaglandin I_2 derivative" from claims 6 and 7, have been added to claim 4. Claim 9 has been amended to update proper claim dependency. In view of the foregoing support, Applicants respectfully request that the Examiner enter the amendments.

II. REJECTION UNDER 35 U.S.C. § 102(b)

The Examiner has rejected claims 4 and 7 as allegedly being anticipated by Hirano *et al.* The Examiner states that Hirano *et al.* teach a compound of instant formula I, which is administered to dogs and then excreted in their urine. The Examiner alleges that the dog's urine would contain ionic compounds. To the extent the rejection is applicable to the amended set of claims, Applicants respectfully traverse the rejection.

As the Examiner is well aware, under M.P.E.P. § 2131, a claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently, in a single prior art reference.

Hirano *et al.* disclose some aspect of the dynamic behavior of the anionic prostaglandin I_2 derivative in the dog. However, the reference fails to disclose that the composition comprising an anionic prostaglandin I_2 derivative and a specified cationic compound as is taught and claimed in the amended claim 4, can show a sustained-releasability *in vivo*. In fact, Hirano *et al.* do not disclose or suggest any pharmaceutical composition. Dog urine is not a sustained release pharmaceutical composition. The pharmaceutical compositions of the present invention are satisfactory for clinical use. (please see page 5, lines 13-16). Dog urine is in no way suitable for clinical use. Accordingly, the Examiner is respectfully requested to withdraw this rejection.

III. REJECTION UNDER 35 U.S.C. § 103(a)

The Examiner has rejected claim 6 as allegedly being obvious over Hirano *et al.* The Examiner states that Hirano *et al.* teach a compound of instant formula I, which is administered to dogs and then excreted in their urine.

Applicants have canceled claim 6 without prejudice or disclaimer. In view of the cancellation of claim 6, this rejection has been rendered moot. Therefore, Applicants respectfully request that the Examiner withdraw the rejection.

IV. ADDITIONAL ART

In a telephone interview on August 18, 2004 between the undersigned representative and the Examiner, the Examiner mentioned two references, which Applicants now put on the record and also distinguish.

A. U.S. Patent No. 5,756,553 ("the '553 patent")

This reference discloses a medical material comprising a (co)polymer having a polar group, wherein the (co)polymer contains an antiplatelet agent, and the medical material is formed (molded) into a proper form. According to the description on column 3, line 43 to column 4, line 9 of the '553 patent, prostaglandin E_1 is described as one of the usable antiplatelet

agents. However, the (co)polymer is used in principle as a material for artificial organs such as heart and the like or a medical instrument such as catheter and the like, but it is neither an anionic compound nor a cationic compound.

In stark contrast, the present invention resides based on the finding that the addition of a certain kind of counter ions to a pharmaceutical composition containing an ionic pharmaceutically effective ingredient can attain sustained release. In this respect, the Examiner's attention is respectfully directed to page 8, lines 3 to 16 of the present specification, which is repeated here for the Examiner's convenience:

> The sustained-release pharmaceutical composition of the present invention is characterized in that by adding a particular counter ion to the ionic prostanoic acid derivative to increase the oil/water partition coefficient of the ionic pharmaceutically active substance, a hydrophobic property is imparted to give the sustained-release pharmaceutical composition of the invention suitable for, e.g., injection. The sustained release according to the present invention is effected by means of a novel method quite different from conventional techniques adopted to control the release of ionic pharmaceutically active substances, to insolubilize a pharmaceutically active substance itself, to retard the dissolution of the active substance by microencapsulation, etc. Moreover, the present invention is characterized in that the sustained release can be achieved by the composition of the invention to a fully satisfactory extent that was obtained only insufficiently by these known means.

Thus, it is apparent that the '553 is entirely irrelevant to the present invention.

B. U.S. Patent No. 6,232,343 ("the '343 patent")

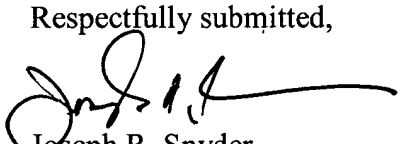
Formulation Example 6 of the '343 is directed to a composition wherein sodium beraprost and phosphates are jointly used. However, the ionic compound in claim 4 is now limited to a cationic compound. That is, there is no overlap in the ingredients in the composition between the present composition claimed in claim 4 and the composition illustrated in Formulation Example 6. Indeed, neither α-cyclodextrin nor chlorobutanol are even ionic compounds.

Formulation Example 7 is directed to a composition wherein sodium beraprost and benzalkonium chloride are jointly used. Benzalkonium chloride is illustrated as one of the counter-ionic compounds in the present invention. However, the amount of the benzalkonium chloride used therein is quite low to express the function as a counter-ionic compound. This is, because the benzalkonium chloride is used in this formulation as a disinfectant, like chlorobutanol in Formulation Example 6. In this respect, please note that the amount of benzalkonium chloride used as a disinfectant is far lower than the *equi-molar amount* of the benzalkonium chloride as is presently claimed.

That is, the formulations illustrated in the '343 patent are given merely to exemplify a typical ophthalmic formulation containing a kind of the prostaglandin I_2 derivative as an effective ingredient. Indeed, this reference is quite silent as to the sustained release of the effective ingredient. Moreover, there is no suggestion as to the necessity of incorporating a certain kind of counter ion into a pharmaceutical composition containing an ionic pharmaceutically effective ingredient in at least an equi-molar for the attainment of the sustained release of the pharmaceutically effective ingredient, such as for example, an anionic prostaglandin I_2 derivative.

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. Applicants respectfully request that the Examiner send this application to issue.

Respectfully submitted,



Joseph R. Snyder
Reg. No. 39,381

TOWNSEND and TOWNSEND and CREW LLP
Two Embarcadero Center, Eighth Floor
San Francisco, California 94111-3834
Tel: 925-472-5000
Fax: 415-576-0300
JS:jc
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